

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number
WO 2004/092213 A1

(51) International Patent Classification⁷: **C07K 14/47, G01N 33/574**

(21) International Application Number:
PCT/US2004/010588

(22) International Filing Date: **5 April 2004 (05.04.2004)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
60/461,399 8 April 2003 (08.04.2003) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

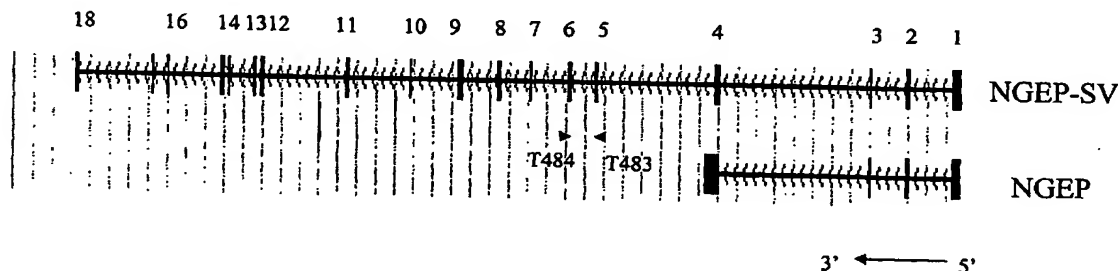
Published:

— with international search report
— with amended claims

Date of publication of the amended claims: 6 January 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **GENE EXPRESSED IN PROSTATE CANCER, METHODS AND USE THEREOF**



(57) Abstract: A polypeptide is disclosed that is specifically detected in the cells of the prostate, termed Splice Variant-Novels Gene Expressed in Prostate (SV-NGEP). Polynucleotides encoding SV-NGEP are also disclosed, as are vectors including these polynucleotides. Host cells transformed with these polynucleotides are also disclosed. Antibodies and immunoconjugates are disclosed that specifically bind SV-NGEP. Methods are disclosed for using an NGEP polypeptide, an antibody that specifically binds SV-NGEP, or a polynucleotide encoding SV-NGEP. Assays are disclosed for the detection prostate cancer. Pharmaceutical compositions including an SV-NGEP polypeptide, an antibody that specifically binds SV-NGEP, or a polynucleotide encoding SV-NGEP are also disclosed. These pharmaceutical compositions are of use in the treatment of prostate cancer.

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AMENDED CLAIMS

[Received by the International Bureau on 15 November 2004 (15.11.04):
original claims 1-46 replaced by amended claims 1-46 (6 pages)]

CLAIMS

1. An isolated polypeptide comprising:
 - (1) an amino acid sequence at least 90% homologous to SEQ ID NO: 1;
 - 5 (2) at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1, wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule; or
 - (3) an amino acid sequence set forth as SEQ ID NO: 1.
- 10 2. The isolated polypeptide of claim 1, comprising a polypeptide having an amino acid sequence at least 90% homologous to SEQ ID NO: 1.
3. The isolated polypeptide of claim 2, comprising an amino acid sequence at least 95% homologous to SEQ ID NO: 1.
- 15 4. The isolated polypeptide of claim 1, comprising at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1, wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule.
- 20 5. The isolated polypeptide of claim 1, comprising an amino acid sequence as set forth as SEQ ID NO: 1.
6. An isolated nucleic acid sequence encoding the polypeptide of claim 1.
- 25 7. The isolated nucleic acid sequence of claim 6, comprising a sequence as set forth as SEQ ID NO: 2, or a degenerate variant thereof.
8. The isolated nucleic acid sequence of claim 6, operably linked to a promoter.
- 30 9. An expression vector comprising the nucleic acid sequence of claim 6.

10. A host cell transfected with the nucleic acid sequence of claim 6.
11. The host cell of claim 10, wherein the host cell is a mammalian cell.
12. An antibody that specifically binds the polypeptide of claim 1.
13. The antibody of claim 12, wherein the antibody is a monoclonal antibody.
14. The antibody of claim 12 comprising a detectable label.
15. The antibody of claim 12, wherein the label is a fluorescent, enzymatic or radioactive label.
16. The antibody of claim 12 conjugated to a toxin.
17. A method for detecting prostate cancer in a subject, comprising
contacting a sample obtained from the subject with the antibody of claim
12 for a sufficient amount of time to form an immune complex;
detecting the presence the immune complex, wherein the presence of an
immune complex demonstrates the presence of prostate cancer in the subject.
18. The method of claim 17, wherein the sample is a biopsy, blood, serum, or
urine sample.
19. The method of claim 17, wherein the sample is a biopsy sample of non-
prostate origin.
20. The method of claim 17, wherein the antibody is labeled.

21. A method for detecting a prostate cancer in a subject, comprising
detecting the expression of the polypeptide of claim 1 in a sample from the
subject, wherein an increase in the expression of the polypeptide as compared to a
control indicates the presence of the prostate cancer.

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22. The method of claim 21, wherein detecting the expression of polypeptide
comprises detecting a polypeptide having a sequence set forth as SEQ ID NO: 2 in the
sample.

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23. The method of claim 22, wherein detecting the expression of the
polypeptide comprises
contacting the sample with an antibody that specifically binds the polypeptide
for a sufficient amount of time to form an immune complex; and
detecting the presence of the immune complex.

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24. The method of claim 21, wherein detecting the expression of the
polypeptide comprises detecting the presence of mRNA encoding the polypeptide.

25. The method of claim 24, wherein detecting the presence of mRNA encoding
the polypeptide comprises a Northern Blot analysis, an RNA Dot blot, or a reverse
transcriptase polymerase chain reaction (RT-PCR) assay.

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26. A method for producing an immune response against a cell expressing a
polypeptide of claim 1 in a subject, the method comprising
administering to the subject a therapeutically effective amount of the
polypeptide of claim 1, or a polynucleotide encoding the polypeptide, thereby
producing the immune response.

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27. The method of claim 26, wherein the immune response is a T cell response.

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28. The method of claim 26, wherein the immune response is a B cell response.

29. The method of claim 26, wherein the subject has prostate cancer.

5 30. The method of claim 29, wherein the immune response decreases the growth of the prostate cancer.

31. A method for inhibiting the growth of a malignant cell expressing the polypeptide of claim 1, the method comprising,

10 (i) culturing cytotoxic T lymphocytes (CTLs) or CTL precursor cells with the polypeptide of claim 1 to produce activated CTLs or CTL precursors that recognize an NGEP expressing cell, and

 (ii) contacting the malignant cell with the activated CTLs or CTLs matured from the CTL precursors,

15 thereby inhibiting the growth of the malignant cell.

32. A method for inhibiting the growth of a malignant cell, comprising:

 contacting the malignant cell with an effective amount of a cell-growth inhibiting molecule, wherein the cell growth inhibiting molecule comprises an antibody
20 which specifically binds a polypeptide comprising

 (1) an amino acid sequence at least 90% homologous to SEQ ID NO: 1;

 (2) at least eight consecutive amino acids of amino acids 157-933 of SEQ ID NO: 1, wherein the isolated polypeptide is eight to ten amino acids in length and binds an MHC molecule; or

25 (3) an amino acid sequence set forth as SEQ ID NO: 1;

 wherein the antibody is covalently linked to an effector molecule which inhibits the growth of cells,

 thereby inhibiting the growth of the malignant cell.

33. The method of claim 32, wherein said antibody is a monoclonal antibody.

34. The method of claim 32, wherein the effector molecule is a
chemotherapeutic agent.

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35. The method of claim 32, wherein the effector molecule comprises a toxic moiety.

36. The method of claim 35, wherein the toxic moiety is selected from the group consisting of ricin A, abrin, diphtheria toxin or a subunit thereof, *Pseudomonas* exotoxin or a portion thereof, saporin, restrictocin or gelonin.

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37. The method of claim 35, wherein the *Pseudomonas* exotoxin is selected from the group consisting of PE35, PE37, PE38, and PE40.

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38. The method of claim 35, wherein the malignant cell is *in vivo*.

39. A pharmaceutical composition comprising a therapeutically effective amount of the polypeptide of claim 1 in a pharmaceutically acceptable carrier.

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40. A pharmaceutical composition comprising a therapeutically effective amount of the polynucleotide of claim 6 in a pharmaceutically acceptable carrier.

41. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 12 in a pharmaceutically acceptable carrier.

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42. A method for reducing the number of prostate cancer cells in a subject, comprising

administering to the subject a therapeutically effective amount of the polypeptide of claim 1, wherein the administration of the NGEF results in an immune response to NGEF,

thereby reducing the number of prostate cancer cells in the subject.

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43. A method for reducing the number of prostate cancer cells in a subject, comprising

administering to the subject a therapeutically effective amount of the polynucleotide of claim 6, wherein the administration of the polynucleotide results in an immune response,

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thereby reducing the number of prostate cancer cells in the subject.

44. A method for reducing the number of prostate cancer cells in a subject, comprising

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administering to the subject a therapeutically effective amount of the antibody of claim 16,

thereby reducing the number of prostate cancer cells in the subject.

45. A kit for detecting an polynucleotide encoding NGEF in a sample, comprising

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an isolated nucleic acid sequence of at least ten nucleotides in length that specifically binds to SEQ ID NO: 2 under highly stringent hybridization conditions; and instructions for the use of the isolated nucleic acid sequence.

46. A kit for detecting an NGEF polypeptide in a sample, comprising an monoclonal antibody that specifically binds to an antigenic epitope of SEQ ID NO: 1; and instructions for the use of the antibody.

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